Genetic riddle solved by kangaroo and platypus

November 1 2006

Australian scientists have unravelled a mystery of the origins of two debilitating human genetic diseases by studying the kangaroo and platypus genome.

The ANU researchers studied the genes that are abnormal in Prader-Willi Syndrome (PWS), which causes abnormal feeding behaviour leading to an initial failure to suck, followed by voracious eating; and Angelman Syndrome (AS), which is marked by severe mental retardation and inappropriate laughter.

Both of these diseases are caused by an error in 'imprinted' genes. Imprinted genes are peculiar, because some work only if they come from the father, and others only if they're from the mother. For nearly all of these genes, both mother's and father's copies work to make protein, providing good backup in case one gene is mutated or deleted.

But for about 70 imprinted genes, only one copy works at least in some organs, tissues or stages of development. If this copy is mutated or deleted, it causes genetic disease. Prader-Willi Syndrome results if the gene copy from the father is mutated or deleted, because the copy from the mother cannot substitute. The opposite is true for Angelman Syndrome.

The ANU student team of Rob Rapkins and Tim Hore, from Professor Jenny Graves' laboratory at the Research School of Biological Sciences, built on the work La Trobe University graduate Megan Smithwick to

investigate the origin of these two human diseases in kangaroos and platypus. These two Aussie animals are good models for studying reproduction genetics because they both have very different reproduction systems – kangaroos bear very tiny live young without foetal development and platypus lay eggs.

“In both the kangaroo and platypus we found the AS gene but not the PWS gene,” Professor Graves said. “The big surprise was that the AS gene turned out to be next to completely different genes from those that are near it in the human genome. The PWS gene and other imprinted genes from the cluster also have no copy in either the kangaroo or platypus.”

Using ‘hard molecular slog’ the team tracked the origin of the Prader-Willi Syndrome gene down to a duplicate of a non-imprinted gene in another part of the genome. With colleagues in Melbourne, Rob and Tim showed that, unlike in humans and mouse, neither gene was imprinted in kangaroos or platypus, showing that they evolved in humans more recently than had been thought.

“Imprinting was thought to have evolved when mammals abandoned egg-laying 210 million years ago, but the absence of the imprinted genes also in kangaroos indicates that imprinting of these genes developed in placental mammals much more recently.

“The imprinted domain seems to have been thrown together from bits and pieces taken from all around the genome and this happened relatively recently in evolutionary terms,” Professor Graves said. “This research sheds new light on the accidental way that imprinted regions can come into being, and suggests evolution of imprinting is an ongoing process in all mammals that bear live young, including humans.”

This research was published in the latest edition of the scientific journal

PLoS Genetics.

Source: Australian National University